(12) INTERNATIONAL A LICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization

International Bureau



20 JUN 2005

(43) International Publication Date 15 July 2004 (15.07.2004)

PCT

(10) International Publication Number WO 2004/058266 A1

(51) International Patent Classification⁷: A61K 31/497, C07D 403/00

(21) International Application Number:

PCT/US2003/040114

(22) International Filing Date:

16 December 2003 (16.12.2003)

(25) Filing Language:

60/469,315

English

(26) Publication Language:

English

(30) Priority Data: 60/435,389 20 Dec

20 December 2002 (20.12.2002) US 9 May 2003 (09.05.2003) US

- (71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): DUFFY, Joseph, L. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). EDMONDSON, Scott, D. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). KIM, Dooseop [KR/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). KIRK, Brian, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

WANG, Liping [CN/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). WEBER, Ann, E. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

- (74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 3-AMINO-4-PHENYLBUTANOIC ACID DERIVATIVES AS DIPEPTIDYL PEPTIDASE INHIBITORS FOR THE TREATMENT OR PREVENTION OF DIABETES

(57) Abstract: The present invention is directed to 3-amino-4-phenylbutanoic acid derivatives which are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/40114

A. CLA	SSIFICATION OF SUBJECT MATTER					
IPC(7) : A61K 31/497; C07D 403/00						
US CL : 514/254.05, 254.06; 544/366, 370						
According to	International Patent Classification (IPC) or to both	national cla	ssification and IPC	i		
B. FIEL	DS SEARCHED					
Minimum documentation searched (classification system followed by classification symbols)						
U.S.: 514/254.05, 254.06; 544/366, 370						
	, 25, 2 , 11.000, 2 , 5					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched						
				i		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)						
Please See Continuation Sheet						
C. DOC	UMENTS CONSIDERED TO BE RELEVANT					
Category *	Citation of document, with indication, where a	nnronrista	of the relevant negation	Polonia de la SV		
A	ASHWORTH et al. 4-CYANOTHIAZOLIDIDES	AC VEDV	OTENT OTABLE	Relevant to claim No.		
	INHIBITORS OF DIPEPTIDYL PEPTIDASE IV.	no veki i "Ricorgani	c and Medicinal Chamister	1-33		
	Letters. 19 November 1996, Vol. 6, No. 22, pages	2745-2748	the whole document	Į		
	pugo.	2. 10 2. 10	, are whole wountent.	Ī		
		•				
	<u>.</u>					
			1	ſ		
				Į.		
		-				
			Ì	•		
	'		j			
<u></u>						
Further	documents are listed in the continuation of Box C.		See patent family annex.			
* S	pecial categories of cited documents:	"T"	later document published after the inter	national filing date or priority		
"A" document	defining the general state of the art which is not considered to be		date and not in conflict with the applica	ation but cited to understand the		
of particu	lar relevance		principle or theory under ing the inver	ntion		
"E" earlier an	nication or natent nublished on or often the International St.	"X"	document of particular relevance; the c	laimed invention cannot be		
	plication or patent published on or after the international filing date		considered novel or cannot be considered when the document is taken alone	ed to involve an inventive step		
	which may throw doubts on priority claim(s) or which is cited to					
specified)	he publication date of another citation or other special reason (as	"Y"	document of particular relevance; the c	laimed invention cannot be		
• •	makambanas an and that		considered to involve an inventive step combined with one or more other such	documents, such combination		
	referring to an oral disclosure, use, exhibition or other means		heing obvious to a person skilled in the	art		
"P" document	published prior to the international filing date but later than the	"& "	document member of the same patent fa	amily		
	ate claimed		•	_		
Date of the a	ctual completion of the international search	Date of mailing of the international search report				
		Date of mailing of the international search report 0 2, JUN 2004				
14 April 2004 (14.04.2004)		U W, J U I Y L U U T				
Name and mailing address of the ISA/US		Authorized officer				
Mail Stop PCT, Attn: ISA/US Commissioner for Patents		Zachary C. Tucker F Rile to In				
P.O. Box 1450		Authorized officer Zachary C. Tucker A. Robe to for				
Alexandria, Virginia 22313-1450			No. (571) 272-1600	//		
Facsimile No. (703)872-9306				Ì		

Form PCT/ISA/210 (second sheet) (July 1998)

	DOD/ITOON/4014		
INTERNATIONAL SEARCH REPORT	PCT/US03/40114		
and the ori			
_			
I			
Continuation of B. FIELDS SEARCHED Item 2			
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search			
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperszine, dinger			
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	ptidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	etidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	etidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diperation of B. FIELDS SEARCHED Item 3: STN- "USPAT," "EPO," "TRUCTURE SEARCHED ITEM SEARCHED	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
Continuation of B. FIELDS SEARCHED Item 3: STN- "registry" file, structure search EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	otidyl peptidase IV, diabetes		
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper			
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper	etidyl peptidase IV, diabetes		
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper			
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper			
EAST- "USPAT," "EPO," "JPO," "Derwent" search terms: piperazine, diper			

Form PCT/ISA/210 (second sheet) (July 1998)